EXHIBIT 8

EXPERT REPORT
DAVID KESSLER, M.D.

72. In 1970, Congress passed the Controlled Substances Act (CSA).[66] The Act established five schedules that classify substances according to "how dangerous they are, their potential for abuse and addiction, and whether they possess legitimate medical value."[67] The drugs at issue in this Report are scheduled as Schedule II drugs, meaning they have a "high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous."[68]

73. Extended-release opioid products, such as controlled-release morphine sulfate products MS CONTIN and Kadian and controlled-release fentanyl products, were positioned as for use in limited circumstances. Nonetheless, reports and articles on the abuse of controlled release opioids began appearing within a few years of when these drugs began hitting the market in the late 1980s. In 1990, only three years after MS CONTIN was approved, an article was published highlighting the drug's abuse potential.[69] The article noted that in areas such as Cincinnati, MS CONTIN had surpassed hydromorphine 4-mg tablets as the most abused prescription opioid.[70] A 1993 study on the abuse potential of opioids found that 85% of the addicts surveyed had used controlled-release morphine.[71]

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[66] *DEA History in Depth 1970-1975*, DEA, https://www.dea.gov/sites/default/files/2018-07/1970-1975%20p%2030-39.pdf (date last visited Sept. 21, 2018).

[67] *Id.*

[68] *Drug Scheduling*, DEA, https://www.dea.gov/drug-scheduling (date last visited Sept. 21, 2018). Hydrocodone combination products, such as Vicodin, were originally scheduled as Schedule III drugs with moderate to low potential for physical and psychological dependence. As of October 6, 2014, hydrocodone combination products are now Schedule II drugs. Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 163, 49661-49682 (Aug. 22, 2014), https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm

[69] Crews, JC, Denson DD, Recovery of morphine from a controlled-release preparation. A source of opioid abuse. *Cancer*. 1990 Dec 15;66(12):2642-4.

[70] *Id.*

[71] Brookoff D, Abuse potential of various opioid medications. *J Gen Intern Med.* 1993 Dec; 8(12):688-90.

74. The lessons learned in the early 20th Century regarding the risks of opioid abuse were pushed aside by the aggressive marketing of a new generation of opioids starting in the 1990s, and opioid manufacturers' understatement of their risks and overstatement of their benefits as set forth below.

V. PURDUE

A. Overview

75. Purdue has promoted and sold various opioid products, including MS Contin and OxyContin.[72]

76. OxyContin is oxycodone in an extended release (ER) tablet, and oxycodone is a full opioid agonist that is relatively selective for the mu receptor.[73]

77. Purdue received initial FDA approval to market OxyContin on December 12, 1995. A discussion of subsequent labeling changes, including approval of OxyContin reformulated, is contained in Schedule 12.

78. In reviewing OxyContin, the FDA Medical Reviewer, Dr. Curtis Wright, IV, approached the review as evaluating an existing drug with a new dosage form. Oxycodone had been on the market as a stand-alone and combination drug that was administered every four to six hours. As noted in the above historical background section, the 1980s and 1990s saw the development of extended release delivery forms for a number of drug entities, including opioids. The review of the OxyContin NDA thus focused primarily on whether the twelve-hour administration was equivalent to the shorter acting immediate-release oxycodone formulation. The longest controlled clinical studies that were submitted as part of the OxyContin NDA were

[72] Other opioid products marketed by Purdue include Butrans, Dilaudid, Dilaudid-HP, Hysingla ER, Targiniq ER.

[73] PPLPC018001498098 at 3.

for fourteen days.[74] Dr. Wright concluded that OxyContin was similar in efficacy and safety to immediate release oxycodone.[75]

79. Notwithstanding that FDA's review primarily focused on the safety and efficacy of this new dosage formulation, Purdue engaged in a marketing and promotional strategy "to change the way pain is treated in America."[76]

80. Prior to the marketing of OxyContin, certain individual healthcare providers, such as Drs. James Campbell, June Dahl, Kathleen Foley, Michael Miller, and Russell Portenoy, advocated for improved pain assessment and treatment. However, Purdue's marketing and promotion focused on expanding the market for strong opioids.[77]

81. Purdue acknowledged in 2001 that its promotional activities "contributed to a paradigm shift."[78]

82. This paradigm shift expanded the use of opioids in treating pain,[79] and the concomitant increase in sales of OxyContin and opioid products in general produced *ipso facto* more opioid drugs in interstate commerce.

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[74] PURCHI-000667209 at 41.

CLINICAL STUDIES

Study Name	Indication	N	Comparison	Duration	PK/PD?
Controlled Trials					
OC91-0402A	CANCER	57/54	CR V. IR	5 DAY + / -	
OC91-0402B	CANCER	81/83	CR V. IR	5 DAY + / -	
OC93-0202	CANCER	50	CR V. IR	7 DAY X-O	PK/PD
OC92-1102	CA	44/44/45	10,20 CR V PLC	14 DAY	PK/PD
OC92-1201	LOW BACK	57	CR V. IR	7 DAY X/O	PK/PD
OC88-1105	POSTOP	30/30/30	10,20,30 CR	SINGLE DOSE	none
		30/31/31	IR, PLC PCT		

[75] PURCHI-000667209 at 39, 52-53.

[76] PKY181297965 at 1.

[77] The elements of Purdue's marketing and promotion that focused on expanding the market for strong opioids were investigated and summarized by the United States General Accounting Office in 2003.

[78] PDD1503491667 at 1; *see also* PPLP003409951, PPLP003541889, PPLP004001344.

36. In my opinion, Actavis's promotion of opioids minimized the risks of addiction and abuse.

37. In my opinion, Mallinckrodt falsely promoted Exalgo as safer than other opioid products.

38. In my opinion, Mallinckrodt's sales training misleadingly minimized the risks associated with higher doses of opioids and encouraged sales representatives to make misleading claims regarding abuse deterrence.

39. In my opinion, Mallinckrodt misleadingly minimized the risk of addiction and funded the CARES Alliance which likewise understated the risk of addiction.

40. In my opinion, Mallinckrodt misleadingly told healthcare providers and trained its sales force that patients exhibiting signs of addiction were likely "pseudoaddicted" and in need of additional opioids to treat pain.

41. In my opinion, Mallinckrodt falsely marketed Xartemis as having a lower potential for abuse as compared to other opioid products.

42. In my opinion, through the pain advocacy group guidelines and materials they helped develop and disseminate, opioid manufacturers contributed to altering the standard of care for the treatment of pain by encouraging healthcare providers to view pain as a "fifth vital sign" that demanded aggressive treatment with opioids.

43. In my opinion, opioid manufacturers' support for and involvement with pain advocacy, professional medical and trade group organizations expanded the use of opioids and increased the risk of abuse.

44. In my opinion, the promotional violations discussed above endanger public health because they encourage the use of opioids in circumstances other than those in which the drugs have been approved, overstate their benefits and minimize their risks.

45. In my opinion, because the promotional violations discussed in this report are serious, corrective promotion and medical education that disseminates truthful, non-misleading, and complete corrective messaging about the violations discussed above to the audiences that received the violative promotion is warranted.

46. In my opinion, the need for corrective promotion here is supported by research that has demonstrated that similar corrective promotion can be effective in countering false and misleading statements made about prescription drug products.

47. In my opinion, manufacturers should assure that no claims, including any superiority claims, about opioids are made without validation of those claims by high quality and well controlled clinical studies.

48. In my opinion, to correct the results of past practices, manufacturers should not fund treatment guidelines, organizations that issue treatment guidelines, or any authors of guidelines that concern pain, opioids or addiction. Disclosure of past and present funding from manufacturers to organizations and individuals that issue or author treatment guidelines should also be made.

49. Based on the totality of the above, it is my opinion that the manufacturers' departures from FDA standards would be expected to (and likely did) have an affect on how healthcare providers prescribed opioids, contributing to a shift in the practice of medicine with regards to the use of opioids in the treatment of pain. This change in the practice of medicine led to an increase in opioid prescriptions, an increase of opioids in interstate commerce, and an

increase in inappropriate use of opioids, all of which in turn increased the risk of opioid abuse and contributed to a public health crisis.

March 25, 2019

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